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| <b>Application Number</b>     | <b>09/402,820</b>       |
| <b>Filing Date</b>            | <b>October 12, 1999</b> |
| <b>First Named Inventor</b>   | <b>CHAIN, Daniel G.</b> |
| <b>Group Art Unit</b>         | <b>1543</b>             |
| <b>Examiner Name</b>          | <b>P. Duffy</b>         |
| <b>Attorney Docket Number</b> | <b>P-4815-US</b>        |

Sheet

1

of

4

Attorney Docket Number

**P-4815-US**

## U.S. PATENT DOCUMENTS

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|  |   | Examiner Name            | P. Duffy         |
|  |   | Attorney Docket Number   | P-4815-US        |
| Sheet  | 3   | Of                       | 4                |
| AZ   | SOLOMON, Beka et al., "Disaggregation of Alzheimer Beta-amyloid by site-directed mAb.", PROC. NATL. ACAD. SCI. USA, vol. 94, pp 4109-4112 (1997)  |                          |                  |
| BA   | TSUZUKI et al., "amyloid beta protein in rot soleus muscle in chloroquine-induced myopathy using end-specific antibodies for A beta 40 and A beta 42: immunohistochemical evidence for amyloid beta protein", <u>Neurosci Letters</u> 202 (1-2):77-80 (1995)                              |                          |                  |
| BB   | TURNER et al., "Mayloids $\beta$ 40 and $\beta$ 42 Are Generated Intracellularly in Cultured Human Neurons and Their Secretion Increases with maturation", <u>J Biol Chem</u> 271 (15):8966:8970 (1996)   |                          |                  |
| BC   | YANAGISAWA et al., "Fractionation of Amyloid $\beta$ protein ( $A\beta$ ) in Alzheimer's Disease and Down's Syndrome Brains: Presence of Membrane-Bound $A\beta$ ", <u>Ann NY Acad Sci</u> 786:184-194 (1996)   |                          |                  |
| BD   | GRAVINA et al., "Amyloid $\beta$ Protein ( $A\beta$ ) in Alzheimer's Disease Brain: Biochemical and Immunocytochemical Analysis with Antibodies Specific for Forms Ending at $A\beta$ 40 or $A\beta$ 42(43)", <u>J Biol Chem</u> 270 (13): 7013-7016 (1995)                               |                          |                  |
| BE   | HARRINGTON et al., "Characterisation of an epitome specific to the neuron-specific isoform of human enolase recognized by a monoclonal antibody raised against a synthetic peptide corresponding to the C-terminus of $\beta$ A-protein", <u>Biochim Biophys Acta</u> 1158:120-127 (1993) |                          |                  |
| BF   | HIGGINS et al., "Transgenic Mouse Brain Histopathology Resembles Early Alzheimer's Disease", <u>Ann Neurol</u> 35:598-607 (1994)  |                          |                  |
| BG   | IWATSUBO et al., "Visualization of $A\beta$ 42 (43) and $A\beta$ 40 in Senile Plaques with End-Specific $A\beta$ Monoclonals: Evidence that an Initially Deposited species is $A\beta$ 42(43) <u>Neuron</u> 13:45-53 (1994)   |                          |                  |
| BH   | IWATSUBO et al., "Amyloid $\beta$ protein ( $A\beta$ ) Deposition: $A\beta$ 42 (43) Precedes $A\beta$ 40 in Down Syndrome". <u>Ann Neurol</u> 37:294-299 (1995)   |                          |                  |
| BI   | KONIG et al., "Development and Characterization of a Monoclonal Antibody 369. 2B Specific for the Carboxyl-Terminus of the $\beta$ A4 Peptide", <u>Ann NY Acad Sci</u> 777:345-355 (1996)   |                          |                  |
| BJ   | MANN et al., "The extent of amyloid deposition in brain in patients with Down's Syndrome does not depend upon the apolipoprotein E genotype", <u>Neurosci Letters</u> 196 (1-2):105-108 (1995)  |                          |                  |
| BK   | MANN et al., "Predominant Deposition of Amyloid $\beta$ 42 (43) in Plaques in Cases of Alzheimer's Disease and Hereditary Cerebral Hemorrhage Associated with Mutations in the Amyloid Precursor Protein Gene", <u>Am J Pathol</u> 148 (4):1257-1265 (1996)                               |                          |                  |
| BL   | MANN et al., "Amyloid beta protein (Abeta) deposition in chromosome 14-linked Alzheimer's diseases: predominance of Abeta 43 (43) <u>Ann Neurol</u> 40 (2):149-156 (1996)   |                          |                  |
| BM   | MURPHY et al., "Development of a Monoclonal Antibody Specific for the COOH-Terminal of $\beta$ -Amyloid 1-42 and Its Immunohistochemical reactivity in Alzheimer's Disease and Related Disorders", <u>Am J Pathol</u> 144 (5):1082-1088 (1994)  |                          |                  |
| BN   | NAKAMURA et al., "Carboxyl end-specific monoclonal antibodies to amyloid beta protein (A beta) subtypes (A beta 40 and A beta 42 (43) differentiate A beta in senile plaques and amyloid angiopathy in brains of aged cynomolgus monkeys." <u>Neurosci Letters</u> 201(2):151-154 (1996)  |                          |                  |

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| <b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b> |                       |  |                          |
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| Examiner Initials*                                       | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (where appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>2</sup>           |
| OL   | AJ                    | BUSCIGLIO J, ET AL, (1193) "Generation of b-amyloid in the secretory pathway in neuronal and nonneuronal cells" Proc. Natl. Acad. Sci. 90, 2092-2096   | <input type="checkbox"/> |
| OL   | AK                    | GEGEDDES JW ET AL. (1999) "N-terminus truncated b-amyloid peptides and C-terminus truncated secreted forms of of anyloid precursor protein: distinct roles in the pathogenesis of Alzheimer's disease" Neuobiol of Aging 20, 75-79.                              | <input type="checkbox"/> |
| OL   | AL                    | HAAS C ET AL. (1992) "Amyloid b-peptide is produced by cultured cells during normal metabolism" Nature 359, 322-325  | <input type="checkbox"/> |
| OL   | AM                    | HAAS C ET AL. (1993)"Cellular processing of β amyloid precursor protein and the genesis of amyloid β-peptide." Cell 75, <1039-1042   | <input type="checkbox"/> |
| OL   | AN                    | HIGGINS LS ET AL. (1996) "p3 b amyloid peptide has a unique and potentially pathogenic immunohistochemical profile in Alzheimer's disease brain." Am. J. Pathol 149, 585-596   | <input type="checkbox"/> |
| OL   | AO                    | JOHNSON-WOOD K. ET AL. "Amyloid precursor protein processing and A beta42 deposition in a transgenic mouse model of Alzheimer disease" Proc Natl. Acad. Sci U.S.A. 1997 Feb 18;94 (4): 1550-5  | <input type="checkbox"/> |
| OL   | AP                    | LALOWSKI M (1996) "The nonamyloidogenic p3 fragment (amyloid β 17-42) is a major constituent of Down's syndrome cerebeller preamyloid." J Biol Chem 271, 33623-31  | <input type="checkbox"/> |
| OL   | AQ                    | LARNER AJ (1999) "Hypothesis: amyloid b peptides truncated at the N-terminus contribute to the pathogenesis of Alzheimer's disease." Neurol. Of Aging 20, 65-69.   | <input type="checkbox"/> |
| OL   | AR                    | MASTERS CL ET AL. (1985) "Amyloid plaque core protein in Alzheimer's disease and Down syndrome." Proc. Natl. Acad. Sci. 82, 4245-9   | <input type="checkbox"/> |
| OL   | AS                    | MILLER DL ET AL. (1994) "Peptide compositions of the cerebrovascular and senile plaque core amyloid deposits of Alzheimer's disease." Archives of Biochemistry and Biophysics 301, 41-52   | <input type="checkbox"/> |
| OL   | AT                    | NASLUND ET AL. (1994) "Relative abundance of Alzheimer Aβ amyloid peptide variants in Alzheimer disease and normal aging." Proc. Natl. Acad. Sci. USA 91, 8378-8382  | <input type="checkbox"/> |
| OL   | AU                    | PIKE CJ ET AL. (1995) "Amino-terminal deletions enhance aggregation of β-amyloid peptides in vitro." J Biol Chem 270, 23895-8  | <input type="checkbox"/> |
| OL   | AV                    | SEUBERT ET AL. (1992) "Isolation and quantification of soluble Alzheimer's β-peptide from biological fluids." Nature 359, 325-327  | <input type="checkbox"/> |
| OL   | AW                    | VIGO-PELFREY C ET AL. (1993) "Characterization of beta-amyloid peptide from human cerebrospinal fluid." J Neurochem 61, 1965-8   | <input type="checkbox"/> |
| OL   | AX                    | HANAN, Ellat et al., "Inhibitory effect of monoclonal antibodies on Alzheimer's Beta-amyloid peptide aggregation" INT. J. EXP. CLIN. INVEST., vol 3, pp. 130-133 (1996).   | <input type="checkbox"/> |
| OL   | AY                    | SOLOMON, Beka et al., "Monoclonal antibodies inhibit in vitro fibrillar aggregation of the Alzheimer Betaamyloid peptide", PROC. NATL. ACAD. SCI. USA, vol. 93, pp 452-455 (1996)  | <input type="checkbox"/> |

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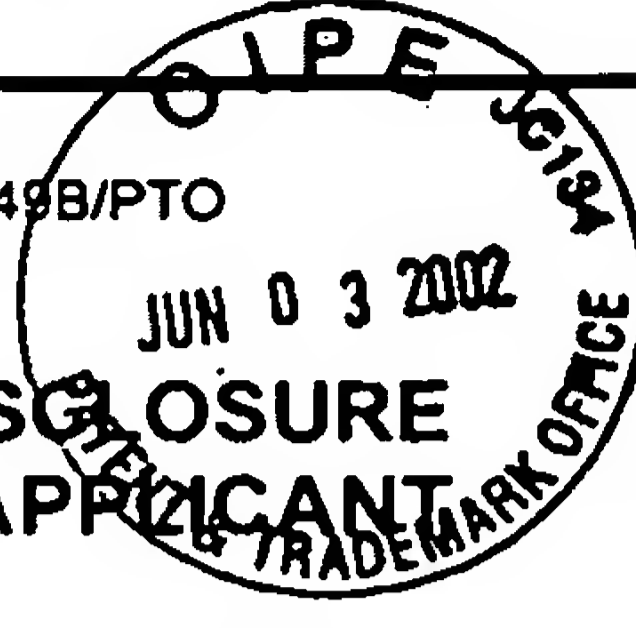
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| <i>ru</i>  | BO               | SAIDO et al., "Spatial Resolution of Fodrin Proteolysis In Postischemic Brain", <u>J Biol Chem</u> 268(33): 25239-25243 (1993)  |   |                    |            |             |                  |                      |                  |                |      |               |          |                        |           |
| <i>ru</i>  | BP               | SUZUKI et al., "High Tissue Content of Soluble $\beta$ 1-40 is Linked to Cerebral Amyloid Angiopathy", <u>Am J Pathol</u> 145 (2):452-460 (1994)  |   |                    |            |             |                  |                      |                  |                |      |               |          |                        |           |
| <i>ru</i>  | BQ               | TAMAOKA et al., "Amyloid $\beta$ protein 1-42/43 ( $A\beta$ 1-42/43) in cerebellar diffuse plaques: enzyme-linked immunosorbent assay and immunocytochemical study", <u>Brain Res</u> 679:151-156 (1995)  |   |                    |            |             |                  |                      |                  |                |      |               |          |                        |           |
| <i>ru</i>  | BR               | DUERIASE et al. <u>Bio Techniques</u> , 16 (3): 436-482   |   |                    |            |             |                  |                      |                  |                |      |               |          |                        |           |
| <i>ru</i>  | BS               | JOHNSON-WOOD K. ET AL., "Amyloid precursor protein processing and A beta42 deposition in a transgenic mouse model of Alzheimer disease," 1997, <u>Proc Natl Acad Sci U S A</u> Feb 18;94(4), pp 1550-5.   |   |                    |            |             |                  |                      |                  |                |      |               |          |                        |           |

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